Complete Summary

GUIDELINE TITLE

Nephropathy in diabetes.

BIBLIOGRAPHIC SOURCE(S)

Molitch ME, DeFronzo RA, Franz MJ, Keane WF, Mogensen CE, Parving HH, Steffes MW. Nephropathy in diabetes. Diabetes Care 2004 Jan;27(Suppl 1):S79-83. [15 references] PubMed

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SCOPE

DISEASE/CONDITION(S)

- Diabetic nephropathy
- Type 1 diabetes mellitus
- Type 2 diabetes mellitus

GUIDELINE CATEGORY

Management
Screening
Treatment

CLINICAL SPECIALTY

Endocrinology
Family Practice
Internal Medicine
Nephrology

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To provide recommendations regarding the detection, prevention, and treatment of early diabetic nephropathy

TARGET POPULATION

- Adult patients with type 2 diabetes mellitus
- Adult patients with type 1 diabetes mellitus who have had diabetes mellitus for over 5 years

INTERVENTIONS AND PRACTICES CONSIDERED

1. Screening for microalbuminuria
2. Intensive diabetes therapy (glycemic control)
3. Hypertension control
    - Lifestyle modifications, such as weight loss, reduction of salt and alcohol intake, and exercise
    - Angiotensin-converting enzyme inhibitor therapy
    - Angiotensin receptor blockers
    - Non-dihydropyridine calcium channel blockers
    - Beta-blockers
4. Protein restriction
5. Sodium and phosphate restriction and the use of phosphate binders

MAJOR OUTCOMES CONSIDERED

- Incidence of end-stage renal disease developing from diabetic nephropathy
- Risk of the development of microalbuminuria and overt nephropathy in people with diabetes
- Rate of progression of nephropathy

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Not stated

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Recommendations have been assigned ratings of A, B, or C, depending on the quality of evidence (see table below). Expert opinion (E) is a separate category for recommendations in which there is as yet no evidence from clinical trials, in which clinical trials may be impractical, or in which there is conflicting evidence. Recommendations with an "A" rating are based on large, well-designed clinical trials or well done meta-analyses. Generally, these recommendations have the best chance of improving outcomes when applied to the population to which they are appropriate. Recommendations with lower levels of evidence may be equally important but are not as well supported.

American Diabetes Association's evidence grading system for clinical practice recommendations:

A

Clear evidence from well-conducted, generalizable, randomized controlled trials that are adequately powered, including:

- Evidence from a well-conducted multicenter trial

- Evidence from a meta-analysis that incorporated quality ratings in the analysis
- Compelling non-experimental evidence, i.e., "all or none" rule developed by the Center for Evidence Based Medicine at Oxford*

Supportive evidence from well-conducted randomized, controlled trials that are adequately powered, including:

- Evidence from a well-conducted trial at one or more institutions
- Evidence from a meta-analysis that incorporated quality ratings in the analysis

*Either all patients died before therapy and at least some survived with therapy, or some patients died without therapy and none died with therapy. Example: use of insulin in the treatment of diabetic ketoacidosis.

B

Supportive evidence from well-conducted cohort studies, including:

- Evidence from a well-conducted prospective cohort study or registry
- Evidence from a well-conducted meta-analysis of cohort studies

Supportive evidence from a well-conducted case-control study

C

Supportive evidence from poorly controlled or uncontrolled studies:

- Evidence from randomized clinical trials with one or more major or three or more minor methodological flaws that could invalidate the results
- Evidence from observational studies with high potential for bias (such as case series with comparison with historical controls)
- Evidence from case series or case reports

Conflicting evidence with the weight of evidence supporting the recommendation

E

Expert consensus or clinical experience

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The paper was peer-reviewed, modified, and approved by the American Diabetes Association's Professional Practice Committee and Executive Committee, November 1996. The paper was most recently reviewed and revised in October 2001.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The evidence grading system (A through C, E) is defined at the end of the "Major Recommendations" field.

General Recommendations

- To reduce the risk and/or slow the progression of nephropathy, optimize glucose control. (A)
- To reduce the risk and/or slow the progression of nephropathy, optimize blood pressure control. (A)

Screening

Perform an annual test for the presence of microalbuminuria in (1) type 1 diabetic patients who have had diabetes >5 years and (2) all type 2 diabetic patients starting at diagnosis. (E)

Treatment

- In the treatment of albuminuria/nephropathy, both angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) can be used:
    - In hypertensive and nonhypertensive type 1 diabetic patients with any degree of albuminuria, ACE inhibitors have been shown to delay the progression of nephropathy. (A)
    - In hypertensive type 2 diabetic patients with microalbuminuria, ACE inhibitors and ARBs have been shown to delay the progression to macroalbuminuria. (A)
    - In patients with type 2 diabetes, hypertension, macroalbuminuria, and renal insufficiency (serum creatinine >1.5 mg/dL), ARBs have been shown to delay the progression of nephropathy. (A)
- If one class is not tolerated, the other should be substituted. (A)
- With regards to slowing the progression of nephropathy, the use of dihydropyridine calcium channel blockers (DCCBs) as initial therapy is not more effective than placebo. Their use in nephropathy should be restricted to additional therapy to further lower blood pressure in patients already treated with ACE inhibitors or ARBs. (B)
- In the setting of the albuminuria or nephropathy, in patients unable to tolerate ACE inhibitors and/or ARBs, consider the use of non-DCCBs, beta-blockers, or diuretics for the management of blood pressure. (E)

- With the onset of overt nephropathy, initiate protein restriction to ≤0.8 g/kg body weight per day (approximately 10% of daily calories), the current adult recommended daily allowance for protein. Further restriction may be useful in slowing the decline of glomerular filtration rate in selected patients.
- If ACE inhibitors or ARBs are used, monitor serum potassium levels for the development of hyperkalemia.
- Consider referral to a physician experienced in the care of diabetic renal disease when the glomerular filtration rate has fallen to either <60 mL/min/1.73 m^2 or difficulties have occurred in the management of hypertension or hyperkalemia.

Definitions:

American Diabetes Association's evidence grading system for clinical practice recommendations:

A

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C

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- Evidence from observational studies with high potential for bias (such as case series with comparison with historical controls)
- Evidence from case series or case reports

Conflicting evidence with the weight of evidence supporting the recommendation

E

Expert consensus or clinical experience

CLINICAL ALGORITHM(S)

An algorithm is provided in the original guideline document for microalbuminuria screening.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are based on recent review articles that discuss published research and issues that remain unresolved. The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Annual screening for microalbuminuria will allow the identification of patients with diabetic nephropathy at a point very early in its course.
- Improving glycemic control, aggressive antihypertensive treatment, and the use of angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers will slow the rate of progression of nephropathy.
- Protein restriction and other treatment modalities such as phosphate lowering may have benefits in selected patients.
- Appropriate antihypertensive intervention can significantly increase the median life expectancy in patients with type 1 diabetes, with a reduction in mortality from 94 to 45% and a reduction in the need for dialysis and transplantation from 73 to 31% 16 years after the development of overt nephropathy.
- Many studies have shown that in hypertensive patients with type 1 diabetes, ACE inhibitors can reduce the level of albuminuria and the rate of progression of renal disease to a greater degree than other antihypertensive agents that lower blood pressure by an equal amount.
- Studies have shown that there is benefit in reducing the progression of microalbuminuria in normotensive patients with type 1 diabetes and normotensive and hypertensive patients with type 2 diabetes.

- Some studies have demonstrated that the non-dihydropyridine calcium channel blocker classes of calcium channel blockers can reduce the level of albuminuria.

POTENTIAL HARMS

- Use of angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) may exacerbate hyperkalemia in patients with advanced renal insufficiency and/or hyporeninemic hypoaldosteronism.
- In older patients with bilateral renal artery stenosis and in patients with advanced renal disease even without renal artery stenosis, ACE inhibitors may cause a rapid decline in renal function. Whether this occurs with ARBs is unknown.
- Cough may also occur with ACE inhibitor use.
- Protein restriction may lead to nutrition deficiency and may be associated with muscle weakness.
- There is no data on ARB use in pregnancy, but they are classified as class C/D.

CONTRAINDICATIONS

CONTRAINDICATIONS

The class of agents including angiotensin-converting enzyme inhibitors is contraindicated in pregnancy and therefore should be used with caution in women of childbearing potential.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- Evidence is only one component of decision-making. Clinicians care for patients, not populations; guidelines must always be interpreted with the needs of the individual patient in mind. Individual circumstances such as comorbid and coexisting diseases, age, education, disability, and above all, patient's values and preferences must also be considered and may lead to different treatment targets and strategies. Also, conventional evidence hierarchies such as the one adapted by the American Diabetes Association may miss some nuances that are important in diabetes care.
- Some evidence suggests that the prepubertal duration of diabetes may be important in the development of microvascular complications; therefore, clinical judgment should be exercised when individualizing these recommendations.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1996 Nov (revised 2001 Oct; republished 2004 Jan)

GUIDELINE DEVELOPER(S)

American Diabetes Association - Professional Association

SOURCE(S) OF FUNDING

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GUIDELINE COMMITTEE

Professional Practice Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Authors of Position Statement, Initial Draft: Mark E. Molitch, MD (chair); Ralph A. DeFronzo, MD; Marion J. Franz, MS, RD, CDE; William F. Keane, MD; Carl Erik Mogensen, MD; Hans-Henrik Parving, MD; Michael W. Steffes, MD, PhD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

The guideline was originally approved in November 1996; the most recent review/revision was completed in 2001.

American Diabetes Association (ADA) position statements are reissued annually.

GUIDELINE AVAILABILITY

Electronic copies: Available from the American Diabetes Association (ADA) Web site.

Print copies: Available from American Diabetes Association, 1701 North Beauregard Street, Alexandria, VA 22311.

AVAILABILITY OF COMPANION DOCUMENTS

The recommendations in this paper are based on the evidence reviewed in the following publications:

- Diabetic nephropathy: etiologic and therapeutic considerations. Diabetes Rev 1995;3:510-64.
- Prevention of diabetic renal disease with special reference to microalbuminuria. Lancet 1995;346:1080-4.
- A description of the American Diabetes Association (ADA) clinical practice recommendations and reports and evidence grading system is available in the introduction to the 2002 compilation: Diabetes Care 2002 Jan;25(Suppl 1):S1-S2.

Print copies: Available from American Diabetes Association (ADA), 1701 North Beauregard Street, Alexandria, VA 22311.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on November 1, 1998. The information was verified by the guideline developer on December 15, 1998. It was updated by ECRI on April 2, 2001, March 14, 2002, July 29, 2003, and March 24, 2004.

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